BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Pan, Yaping

eRA COMMONS USER NAME (credential, e.g., agency login): yp2177

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
School of Medicine, Fudan University, Shanghai, China	B.S.	06/1999	Pharmacology
Peking Union Medical College, Beijing, China	Ph.D.	06/2004	Neuropharmacology
Baylor College of Medicine, Houston, TX	Postdoc	09/2005	Neuroscience
Columbia University, New York, NY	Postdoc	04/2011	Physiology

A. Personal Statement

I am interested in structure and function of ion channels and transporters and seek to understand how these protein machines work at the molecular level. I have extensive trainings in physiology and biophysics, and I am proficient in various biochemical and biophysical approaches.

1. **Pan Y**, Weng J, Kabaleeswaran V, Li H, Cao Y, Bhosle R, Zhou M. Cortisone dissociates *Shaker* family K^+ channels from their β subunits. ***Nature Chemical Biology***, 4(11): 708-714. (2008)
2. Cao Y*****, **Pan Y***, Huang H*****, Jin X, Levin EJ, Kloss B, Zhou M. Gating of the TrkH ion channel by its associated RCK protein TrkA. ***Nature***, 496(7445): 317-322. (2013) (* equal contribution)
3. **Pan Y**, Ren Z, Gao S, Shen J, Wang L, Xu Z, Yu Y, Bachina P, Zhang H, Fan X, Laganowsky A, Yan N, Zhou M. Structural basis of ion transport and inhibition in ferroportin. ***Nature Communications***, 11(1):5686. (2020)
4. Wilbon AS, Shen J, Ruchala P, Zhou M, **Pan Y**. Structural basis of ferroportin inhibition by minihepcidin PR73. ***PLoS Biology***, Jan 17;21(1):e3001936. (2023)
5. Shen J, Wilbon AS, Zhou M, **Pan Y**. Mechanism of Ca^{2+} transport by ferroportin. ***Elife***, Jan 17;12:e82947. (2023)

Current Research Support

1 R01 HL157473-01 Pan (PI) 05/01/2021 – 04/30/2025
NIH/NHLBI
Structure and Mechanism of Mammalian Ferroportin
The major goal of this project is to understand the mechanism of iron transport in ferroportin and its inhibition by hepcidin.
Role: PI

B. Positions, Scientific Appointments, and Honors

Positions and Employment

04/2011-01/2013	Associate Research Scientist, Department of Physiology and Cellular Biophysics, Columbia University, New York, USA
02/2013-06/2014	Research Associate, Department of Biochemistry and Molecular Biology, Baylor College of Medicine, Houston, USA
07/2014-05/2020	Instructor, Department of Biochemistry and Molecular Biology, Baylor College of Medicine, Houston, USA
06/2020-present	Assistant Professor, Department of Biochemistry and Molecular Biology, Baylor College of Medicine, Houston, USA

C. Contributions to Science

1. As a postdoctoral fellow, I studied modulation of Kv1 channels by the associated Kvβ subunit. I demonstrated that Kvβ1 is a functional aldo-keto reductase and that the enzymatic activity of Kvβ modulates the N-type inactivation in Kv1 channels. These results demonstrated direct coupling between an oxidoreductase and ion channel activities and have important implications in cellular oxygen sensing and response to metabolic changes. I then showed that oxidation of a Kvβ-bound cofactor NADPH potentiates channel activity, and that the potentiation comes from release of N-type inactivation. In a parallel project, I designed a high-throughput screen to identify molecules that bind to Kvβ and I found that cortisone binds to Kvβ and reduces channel inactivation. I then showed that cortisone and its analogs promote dissociation of Kvβ from the channel, and providing a novel way of regulating Kv1 channels.

a. **Pan Y**, Weng J, Cao Y, Bhosle R, Zhou M. Functional coupling between the Kv1.1 channel and an aldo-keto reductase Kvbeta1. ***Journal of Biological Chemistry***, 283(13): 8634-8642. (2008)
b. **Pan Y**, Weng J, Kabaleeswaran V, Li H, Cao Y, Bhosle R, Zhou M. Cortisone dissociates *Shaker* family K^+ channels from their β subunits. ***Nature Chemical Biology***, 4(11): 708-714. (2008)
c. **Pan Y**, Weng J, Levin EJ, Zhou M. Oxidation of NADPH inhibits ball-and-chain type inactivation by restraining the chain. ***Proceedings of the National Academy of Sciences***, 108(14): 5885-5890. (2011)
d. **Pan Y**, Levin EJ, Quick M, Zhou M. Potentiation of the Kv1 family K^+ channel by cortisone analogues. ***ACS Chemical Biology***, 7(10): 1641-1646. (2012)

2. When I finished the Kv1-Kvβ project in 2011, the field of ion channel structure and function is transitioning rapidly towards solving structures of ion channels and using the structures as a starting point for developing further mechanistic studies. I started to learn membrane protein expression and purification and worked on a bacterial channel TrkH and a bacterial bile acid transporter. I worked on both the structural and functional aspects of the TrkH project, combining electrophysiology, X-ray crystallography, and more recently cryo-electron microscopy, to first demonstrate that TrkH is an ion channel gated by ATP and ADP, and that the gating is achieved by conformational changes in the attached TrkA protein.

a. Cao Y*****, **Pan Y***, Huang H*****, Jin X, Levin EJ, Kloss B, Zhou M. Gating of the TrkH ion channel by its associated RCK protein TrkA. ***Nature***, 496(7445): 317-322. (2013) (* equal contribution)
b. Zhang H, **Pan Y**, Hu L, Hudson MA, Hofstetter KS, Xu Z, Rong M, Wang Z, Prasad BVV, Lockless SW, Chiu W, Zhou M. TrkA undergoes a tetramer-to-dimer conversion to open TrkH which enables changes in membrane potential. ***Nature Communications***, 11(1):547. (2020)

3. I have worked extensively on the only iron exporter in human, ferroportin (Fpn), with the goal of visualizing the structures and understanding the mechanisms of substrate recognition, transport and inhibition. Fpn adopts a major facilitator superfamily fold, and has two Fe2+ binding site. Functional studies show that Fpn is an electroneutral H+/Fe2+ antiporter. Fpn can also transport Ca2+. Ca2+ binding site is distinct from that of Fe2+. I solved the structure of Fpn in complex with hepcidin, which is an endogenous Fpn inhibitor. Hepcidin binds to Fpn and inhibits its transport activity directly, which is a novel regulation pathway in addition to inducing

internalization and degradation of Fpn by hepcidin. I also solved the structure of Fpn in the presence of PR73, one minihepcidin. The structure reveals novel interactions that were not present between Fpn and hepcidin.

a. **Pan Y**, Ren Z, Gao S, Shen J, Wang L, Xu Z, Yu Y, Bachina P, Zhang H, Fan X, Laganowsky A, Yan N, Zhou M. Structural basis of ion transport and inhibition in ferroportin. ***Nature Communications***, 11(1):5686. (2020)
b. Wilbon AS, Shen J, Ruchala P, Zhou M, **Pan Y**. Structural basis of ferroportin inhibition by minihepcidin PR73. ***PLoS Biology***, Jan 17;21(1):e3001936. (2023)
c. Shen J, Wilbon AS, Zhou M, **Pan Y**. Mechanism of Ca^{2+} transport by ferroportin. ***Elife***, Jan 17;12:e82947. (2023)

Complete List of Published Work in MyBibliography:
https://pubmed.ncbi.nlm.nih.gov/collections/59665745/?sort=date&direction=ascending